UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,620	06/27/2007	Jonni Moore	P-7671-US	5253

49443 7590 11/02/2009

Pearl Cohen Zedek Latzer, LLP
1500 Broadway
12th Floor
New York, NY 10036

EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
11/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,620	MOORE ET AL.	
	Examiner	Art Unit	
	PAUL C. MARTIN	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 6-27* is/are pending in the application.

4a) Of the above claim(s) *14-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3 and 6-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3 and 6-27 are pending in this application, Claims 14-27 are acknowledged as withdrawn, Claims 1, 3 and 6-13 were examined on their merits.

The objection to the Specification for the improper use of the Trademark ORACLE™ has been withdrawn due to the Applicant's amendments to the Specification filed 09/09/09.

The objection to Claim 1 because of a minor spelling informality has been withdrawn due to the Applicant's amendments to the Claims filed 09/09/09.

The rejection of Claims 7 and 8 under 35 U.S.C. § 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention has been withdrawn due to the Applicant's amendments to the Claims filed 09/09/09.

The rejection of pending Claims 1, 6-9, 12 and 13 under 35 U.S.C. § 103(a) as being unpatentable over McCabe *et al.* (2001) in view of Nygaard *et al.* (2002) has been withdrawn due to the Applicant's amendments to the Claims filed 09/09/09.

Drawings

The drawings remain objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Figure 2 (M1 and M2). Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The use of the trademark TO-PRO™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 13 is newly objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Amended Claim 1 now teaches the use of CFSE as the intracellular protein stain.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6 and 8 are newly rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 8 is dependent upon the method of claims 1 and 6 which requires staining a peripheral blood leukocyte (PBL) population obtained from a subject with an intracellular protein stain, wherein said intracellular protein stain comprises carboxy fluorescein diacetate succinimide ester (CFSE);

contacting said population with an amount of a beryllium containing compound sufficient to stimulate or enhance proliferation of said population; and measuring the loss of intracellular protein staining, whereby loss of intracellular protein staining indicates proliferation and that a subject is sensitive to beryllium and further comprising the step of selecting a subpopulation of said peripheral blood leukocyte population using a cell surface marker, wherein said marker is CD8.

However, the Specification clearly states that while there may be a significant difference in response of CD3 and CD3/CD4 T-cells from beryllium-sensitized subjects, no differences were noted in the response of CD8 T-cells from either normal donors or beryllium sensitized individuals consistent with previous reports (Specification, Pg. 25, Lines 1-6). Therefore, as there was no detectable difference between control CD8 levels and beryllium-sensitized individuals it would be impossible to determine beryllium sensitivity in a subject using the instant method and the cell surface marker CD8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3 and 6, 7, 9-13 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Fontenot *et al.* (2003) for reasons of record set forth in the Prior Action.

Response to Arguments

Applicant's arguments filed 09/09/09 have been fully considered but they are not persuasive.

The Applicant argues that the claimed invention is directed to "determining beryllium sensitivity…comprising staining a peripheral blood leukocyte (PBL)…with…CFSE", While Fontenot *et al.* relates to labeling branchoalveolar lavage (BAL) CD4 T-cells with CFSE and that the Examiner asserts without data or support, that one can substitute PBL T-cells for the BAL cells of Fontenot *et al.* (Remarks, Pg. 8, Lines 15-22).

This is not found to be persuasive for the following reasons, Applicant's arguments focus narrowly on one aspect of the teachings of Fontenot *et al.* and do not address the totality of the teachings cited in the last action.

Fontenot *et al.* teaches a method wherein peripheral blood mononuclear cells (PBMCs) and bronchoalveolar lavage (BAL) cells from subjects diagnosed with chronic beryllium disease (CBD) are stained with monoclonal antibodies to CD4, CD8 and CD28 in order to identify the lymphocyte (T-cell) population and contacting the identified BAL T-cell subpopulation with the intracellular protein stain CFSE. PBMCs consist of any blood cell having a round nucleus, for example, monocytes and lymphocytes. All white blood cells (e.g. monocytes and lymphocytes) are by definition, leukocytes. Therefore, Fontenot *et al.* teaches the isolation of both PBL and BAL T-cell populations. As discussed in the Prior Action, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Fontenot *et al.* wherein BAL T-Cells are stained with CFSE in order to measure proliferation due to exposure to beryllium by substituting PBL T-cells (or PBMCs) for BAL cells because the reference teaches the use of both types of cells in beryllium exposure assays and one of ordinary skill in the art would have recognized that the cell types were art-recognized equivalents. The MPEP states:

> In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958)

One of ordinary skill in the art would have been motivated to make this substitution because the inherent advantages of using blood derived lymphocytes as opposed to BAL derived lymphocytes. Obtaining blood lymphocytes only requires a simple draw blood from a subject whereas BAL is a medical procedure requiring passing a bronchoscope through the mouth or nose of a subject and into the lung. There would have been a reasonable expectation of success in making this substitution as the reference teaches the use of both types of lymphocytes.

The Applicant argues that PBL and BAL cells are completely different cell types, that BAL cells contain components of the epithelial lining fluid of lungs (ELF) of lungs and is often used to determine the protein composition of the pulmonary airways or pathogen levels in the lung while PBLs are composed of polymorphonuclear cells, including monocytes as well as lymphocytes (Remarks, Pg. 8, Lines 23-27).

As discussed above, the rejection based upon Fontenot *et al.* was based upon the teachings of the reference of the use of both PBMCs (monocytes and lymphocytes) also acknowledged by Applicant above as PBLs, as well as BAL derived lymphocytes and why it would be obvious to use PBMC lymphocytes as substitutes for BAL derived lymphocytes. The Examiner has provided a reasoned statement as to why this substitution would be both obvious and desirable above.

The Applicant argues that Fontenot relates to only to the antigen-specific CD4 T-cell response to beryllium while the instant application demonstrates CFSE-measured proliferative response for both CD4 and CD8 T-cells to beryllium and that the "finding a beryllium response in a population of…CD8 T-cells was unexpected." Applicant asserts that for this reason the claimed invention is unexpected and unpredictable over the cited reference (Remarks, Pg. 9, Lines 7-14).

This is not found to be persuasive for the following reasons, the citation the Applicant cites (Specification, Pg. 24, Lines 20-24) does not refer to an unexpected result but merely to results of initial experiments wherein it was not possible to distinguish the proliferative response of CD3/CD4 and CD3/CD8 cell populations until anti-CD8 APC was substituted for TO-PRO™-3. The teachings of the Specification clearly state that while there may be a significant difference in response of CD3 and CD3/CD4 T-cells from beryllium-sensitized subjects, no differences were noted in the response of CD8 T-cells from either normal donors or beryllium sensitized individuals consistent with previous reports (Specification, Pg. 25, Lines 1-6).

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

10/28/09

/Rebecca E. Prouty/
Primary Examiner,
Art Unit 1652